extent nor in like manner. For example, in a certain stage of the action of choral upon the heart muscle, its rhythm alone is decreased; its other properties are apparently unaltered. Camphor promptly overcomes this depression and restores the rhythm. Digitalis has a much more complex action. First, it has a very marked stimulant action on the cardio-inhibitory centre and on vagus nerve endings in the heart, and consequently decreases rhythm. Roughly, the higher the rate above normal, the greater this effect is, while if the rate is normal the effect is very slight and even absent. The next most important action seems to be upon the tone and contractivity of the heart muscle acting on its cells directly. The contractivity is increased and more blood, in consequence, expelled at each beat. Its tone is also increased, and hence a decrease in the volume of the cavity of the heart, and decrease of dilatation, if this exists. These two properties also undergo little or no change with therapeutic doses if the heart muscle is normal, while the change is very marked if the heart is dilated. Conductivity is depressed. This is important, for often the first sign of the cumulative action of the drug is due to this fact, and is manifested in the slow ventricular rhythm, while the auricle continues to beat more rapidly (heart block). The action upon the vessels is primarily to increase their tone, and hence increase the blood pressure. This action, however, appears to be slight in therapeutic doses. More recent studies have shown that it tends to dilate the coronary vessels and those of the kidney (Löwy). That we are able to make such a precise statement of the pharmacological action of digitalis is due to the physiological work of Baskell, extended by Engelmann, Langendorff, Hering, Bock, and others, and the pharmacological work of Williams, O. Frank, Gottlieh and Magnus,[1] and Böhme.[2]

The studies of Schmiedeberg, Kiliani, Homolle, Nativelle, and Cloetta have shown us that digitalis contains probably more than one glucoside, and that these glucosides are not stable and are exceedingly difficult to isolate. Such a series of experiments as those of Haynes[3] has forced us to recognize that the active principles are present in very varying amounts in the crude drug when gathered at different times and in different localities, and as a result in the galenical preparations made from them: Hence the necessity for pharmacological standardization.

The work of Fraser,[4] Feist, and Thoms[5] has shown that strophanthus contains an active principle which is similar in its action to digitalis, and differs from it only in being more irritant and somewhat more rapid in its action. This fact has become of great importance since Fraser succeeded in isolating from Strophanthus kombé, an amorphous glucoside whose isolation is easy and which may be readily obtained pure. Thoms has succeeded in isolating from Strophanthus gratus a crystalline glucoside which has similar advantages.

---

[1] Arch. f. exp. Path. u. Pharm. 1905, li, 30.

[2] Ibid., lii, 346.

[3] Biochem. Jour., 1906, i.

[4] Trans. Royal Soc., Edinburgh,.1890.

[5] Pharm. Zeit., lii, 699, cited in the Jahresbericht d. Pharm., 1907, 42.

It was on account of the ease with which a pure strophanthin of known pharmacological activity could be obtained that Fraenkel[6] selected this representative of the digitalis group for intravenous administration. The advantages that he obtained by intravenous injection were, first, the great decrease in time between administration and evident pharmacological action. Strophanthin given per os usually does not act for at least seventeen hours; digitalis often not for thirty-six hours. Subcutaneously strophanthin in just toxic doses acts in four or five hours when administered to a rabbit, while digitalinum requires twenty-four hours or more. Intravenously the action is fully established in thirty to sixty minutes. Secondly, the certainty of absorption; both strophanthin and the glucosides of digitalis are irritant and slowly absorbed in the intestines; there is, in consequence, great danger of irritating the stomach, of increased peristalsis, and in consequence a loss of a varying amount of the dose administered. Owing to the irritant nature of these glucosides, administration per os is often contra-indicated. This property also makes their subcutaneous administration painful; the pain, except the skin prick, when administered intravenously, is, of course, absent. Thirdly, in many cases a single injection will produce as much benefit as a week's treatment with digitalis per os. As in the two cases reported below, a single injection was sufficient completely to restore broken cardiac compensation. The method had this further advantage; that one can tell in an hour or two whether digitalis will aid the case or not; and if it fails, one can try some other procedure without the long wait entailed if administration per os be adopted.

The first case which I report illustrates these points very well:

Case I.—J. McB., aged sixty-five years, has led a worrying life; generally in good health until three years ago, since when he has had several attacks of cardiac weakness. The present attack began about six weeks ago, but has been much worse during the past week, so that the patient has been confined to bed. Status presens: Patient robust, muscular; arteries somewhat sclerosed; pulse, 140 (?); at apex 160 beats were counted, irregular, weak; blood pressure, 160 cm. of water; diastolic pressure, 120 (the measurements were made with a von Recklinghausen sphygmomanometer). Cardiac dulness from one-half inch to the right of the sternum to the midaxillary line. Area of pulsation from one-half inch internal of the mammary line to the midaxillary line in the fourth, fifth, and sixth interspaces. Marked liver pulsation. Liver one inch below the sternum, one and one-half inches below the right costal margin in the mammary line. Some œdema about the ankles. The quantity of urine has been failing, and up to the time of examination, 8 P.M., only two or three ounces has been passed since the preceding evening. Cheyne-Stokes respiration of the following type:

---

[6] Arch. f. exp. Path. u. Pharm. 1904, li, 84; Therap. Monatssch., 1909, xxiii, 109; Arch. f. exp. Path. u. Pharm. 1907, lvii, 79; 1908; Suppl. Bd., 88.

	Pulse.	Systolic pressure.	Diastolic pressure.	Difference.	Work.
December 12, 8.35 P.M.	166	160	120	40	6640
1 mg. of strophanthin intravenously.					
December 12, 8.55 P.M.	150	174	132	42	6300
December 12, 9.30 P.M.	66	180	110	70	4620
December 12, 9.45 P.M.	64	190	100	90	5760
December 12, 11.00 P.M.	60	180	100	80	4800
December 13, 6.00 P.M.	64	188	105	83	5312
December 19	64	185	103	82	5284

At 8.55 the amplitude of the pulse, both felt with the finger and as observed in the swinging of the sphygmomanometer needle, seemed better. At 9.45 several ounces of urine was passed, and urine was passed again at eleven o'clock. On the following day the liver pulsation was absent, though the liver was still palpable and about one-half inch below the right costal margin. The area of cardiac pulsation and dulness was slightly less than it had been. The Cheyne-Stokes respiration had completely disappeared. Beyond rest in bed no other treatment of importance was adopted. A subsequent attack, which came on some months later, was relieved in the same manner.

CASE II.—Female, aged twenty-three years. Has a severe mitral insufficiency, and has suffered on several occasions from broken compensation. The use of digitalis has in all cases been sufficient to restore the compensation in about a week. After some undue exertion the present attack occurred. During the past two days less than eight hundred cubic centimeters of water has been passed, and signs of oncoming œdema are quite manifest about the ankles. When seen on April 30, 1909, there was slight dyspnœa, and the following pressures were noted:

	Pulse.	Systolic pressure.	Diastolic pressure.	Difference.	Work.
April 30, 1909, 4.00 P.M.	132	156	116	40	5280
April 30, 1909, 4.15 P.M.	180	180	114	66	7128
April 30, 1909, 4.45 P.M.	90	176	116	60	5400
April 30, 1909, 6.10 P.M.	88	180	116	64	5632
May 1, 1909, 3.40 P.M.	80	178	112	66	5280

During the twenty-four hours ending on the morning of May 1, four thousand cubic centimeters of urine was passed, and on the subsequent days about fifteen hundred. Rest in bed was sufficient to bring about a restored compensation.

It is hardly necessary to repeat what is well known in regard to the indications for the use of digitalis or of strophanthin as its substitute. It might, however, be of value to point out some of the cases in which a failure to obtain a successful result will be observed. Fraenkel has drawn attention to the fact that a successful use cannot be expected when the cause of the œdema or ascites is entirely due to a kidney trouble, but that digitalis can only aid in these cases when there is a failure of circulation due to secondary cardiac failure. In sepsis or in acute pneumonia, when the intoxication has already become intense, and the pulse has become very rapid and weak, strophanthin has no effect in decreasing the rate or in strengthening the beat.

CASE III.—Mrs. E., aged 45 years. A severe lobar pneumonia, affecting both lungs, with high fever and every sign of marked intoxication; gave premature birth to a child of seven months. At the time of the administration of strophanthin, she had a weak, rapid pulse, which could not be counted at the wrist, but was at least 180 at the apex. Venesection had failed to give relief. No improvement in either rate or force of the heart beat could be observed.

In a case of sepsis supervening after pregnancy, and in a case of septicemia in a child of eleven, equally unsuccessful results were obtained. I might note in passing that many of the clinicians who use digitalis in pneumonia resort to its administration at an early stage of the disease, and von Jaksch[7] advises its use in sepsis as soon as the increase in cardiac rate is observed.

An experiment on a dog which contracted pleuropneumonia while in the laboratory gave an opportunity to repeat the clinical experiments under more favorable conditions. The dog was given morphine, and then pithed; artificial respiration was then undertaken; the chest was opened, cannulæ placed in carotid and jugular, and the ventricle attached to a myograph. Rate, 120; mean pressure, 80; 1 mg. strophanthin intravenously had no effect during the succeeding thirty minutes. The blood pressure fell to 70. The vagi were stimulated, but a strong current was needed to produce any effect. Vagus arrest was not obtained with the current available, and the deduction was made that the vagus effect on the heart was not normal. Further experiments of this type will be carried out in the near future.

I feel that Fraenkel's method of intravenous administration of strophanthin puts into the hands of the physician a very valuable means of overcoming cardiac weakness promptly, and, in consequence, must prove a very great boon. The mode of application is so certain, its effect so striking, that it might almost awake a suspicion that such drastic action might damage the heart. It might be felt that, in order to maintain the circulation when the cardiac rate is so suddenly decreased, a very great increase of work must be done by the heart. This is certainly true for each individual beat, but if one takes the total amount of work done during a unit of time, this is by no means necessarily the case. If one admits that von Recklinghausen[8] is correct in judging the relative amount of work done by the heart by the product of the difference between diastolic and systolic pressure and the rate per minute, the two cases quoted above indicate two of the different results which may be seen. It will be noticed that in the fifth column the product of the difference and the pulse rate is given, and that in the first case a definite decrease in the work done is shown, while in the second case there is at first an apparent rise, though the work finally is by chance identical with that performed by the heart before treatment. We must, however, remember that even if the heart is doing a greater amount of work in each interval of time, we have increased its ability to do work owing to the increase in the contractibility of the muscle cells, and have also decreased the danger of cardiac failure by increasing the tone of the heart muscle. We have also probably improved the nutrient conditions of the muscle, as digitalis increases the flow through the coronary vessels.

---

[7] Therap. Monatssch., 1909, xxiii, 78.

Attention might perhaps be drawn to the results obtained by Pohl[9] and Löwy.[10] The latter showed that if digitalis be given in combination with acid, the glucosides quickly decrease in activity. This is, of course, a well-known type of chemical incompatibility. Pohl has, however, called attention to the danger of pharmacological incompatibility, and has shown that the combination of quinine with digitalis decreases the latter's cardiac action. The same seems to be true of potassium salts and of caffeine, while alcohol, chloroform, and liquor ammoniæ anisatus aids its action. Morphine and codeine seem to decrease the rate of absorption, and hence decrease the effectiveness of the drug stuff.

DIGESTIVE OR ALIMENTARY HYPERSECRETION OF GASTRIC JUICE.[1]

By Julius Friedenwald, M.D.,
PROFESSOR OF GASTRO-ENTEROLOGY IN THE COLLEGE OF PHYSICIANS AND SURGEONS, BALTIMORE.

Digestive or alimentary hypersecretion is a condition in which abnormally large amounts of gastric secretion are obtained after the introduction of an ordinary test meal, although the fasting stomach contains but a few cubic centimeters of juice. The latter finding distinguishes this condition from continuous hypersecretion. This disorder was first described by Straus,[2] who pointed out that in some forms of hyperacidity relatively large quantities of a thin, watery, gastric secretion were obtained one hour after a test breakfast. He attributed this condition to the disturbance of the starch digestion on the ground that the undissolved starch acted as a stimulant to the further secretion of hydrochloric acid. Zweig and Calvo[3] investigated this condition more fully. They employed the Sahli test meal as a means of distinguishing it from other conditions and designated it "Alimentary Hypersecretion." They differentiated alimentary hypersecretion from the larval hyperacidity described by Straus and by Schüler[4] characterized by the following symptoms: (1) The formation of amidulin; (2) an increased amount of stomach contents; (3) a lowered specific gravity; and (4) a lowering of the freezing point.

---

[8] Arch. f. exp. Path. u. Pharm. 1906, lv, 375, 412.

[9] Therap. Monatsschr., 1909, xxiii, 110.

[10] Wien. klin. Woch., 1906, No. 39.

[1] Read at a meeting of the Association of American Physicians, Washington, D. C., May 4, 1910.

The typical symptoms of hyperacidity are present in larval hyperacidity, and yet the contents removed after the test breakfast reveal a normal percentage of free acid. Straus and Schüler assume that in these cases there is actually a hyperacidity, which is not revealed because the examination of the gastric contents is made an hour after the test breakfast has been taken. It is possible that the increased quantity of acid secreted at first (secretio celer et magna) is soon neutralized by the so-called diluting secretion, so that the amount of acid in the test breakfast is found to be normal or subnormal. Elsner[5] working under the direction of Boas, again called attention to this condition, and Boas[6] more recently investigated this question and considers the term digestive gastrosuccorrhœa more appropriate than alimentary gastrosuccorrhœa. This particular form of increased gastric secretion is dependent upon the act of digestion, in contradistinction to continuous hypersecretion in which the secretion extends beyond the digestive act, and in which considerable amounts of gastric juice are found in the fasting stomach. All of the twelve cases reported by Boas occurred in males; the disease is found in youth as well as in old age. An important symptom is the extreme emaciation, a loss of from ten to fifteen pounds in weight being a rather usual occurrence. This loss of flesh is a most important sign, especially since it appears without the slightest tendency to disturbance of motility of the stomach. The appetite and quantity of food consumed may be normal; occasionally, however, both may be decreased. The great loss in weight must depend upon the loss of gastric secretion. Amylolysis is greatly diminished and constipation is very marked. The subjective signs are of much the same character as those found in nervous dyspepsia. Patients complain of various sensations in the stomach, pressure, fulness, eructations,

---

[2] Deut. Archiv f. klin. Med., lvi, 120.

[3] Archiv. f. Verdauungskr., 1903, ix, 262.

[4] Münch. med. Woch., 1898.

[5] Berl. klin. Woch., 1904, 670.

[6] Deut. med. Woch., 1907, 135.

GYNECOLOGY.

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.

The Treatment of Inflammatory Diseases of the Adnexa with Intra-uterine Injections 461
Dysmenorrhœa in Nulliparous Women without Gross Pathological Lesions 462
Histological Studies on the Influence of Röntgen-rays upon the Human and Animal Ovaries 462
The Evidence Afforded by Bacteriological Examinations for Treatment of the Wound in Abdominal Operations for Carcinoma of the Uterus 463
The Occurrence and Complications of Sarcoma of the Ovary . . . 463

OPHTHALMOLOGY.

UNDER THE CHARGE OF

EDWARD JACKSON, A.M., M.D.,

AND

T. B. SCHNEIDEMAN, A.M., M.D.

After-results of Magnet Attractions 464
Scopolamin-Morphine Narcosis 464
Treatment of Sympathetic Ophthalmia by Large Doses of Sodium Salicylate or Aspirin 465
Extraction in the Capsule 465
Tuberculosis of the Lacrimal Sac 465
Etiology of Strabismus 465
Albuminuric Retinitis and Azotemia 465

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

WARFIELD T. LONGCOPE, M.D.,

ASSISTED BY

G. CANBY ROBINSON, M.D.

The Glycyl-Tryptophan Test for Carcinoma of the Stomach . . . 466
The Rapid Diagnosis of Diphtheria by Fixation of the Complement . 466
The Bactericidal Substances Extracted from Normal Leukocytes . . 467
Autolysis of Pneumococci 467
The Cultivation of Tubercle Bacilli from Sputum 468

THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES.

SEPTEMBER, 1910

ORIGINAL ARTICLES.

THE THERAPEUTIC ACTION OF DIGITALIS.

BY V. E. HENDERSON, M.D.,
ASSOCIATE PROFESSOR OF PHARMACY AND PHARMACOLOGY IN THE UNIVERSITY OF TORONTO,
TORONTO, CANADA.

SINCE Withering, in the years 1776 to 1779, by careful observation established the therapeutic powers of digitalis, this drug has formed one of the most valuable weapons which the physician possesses. Withering's directions for its use and his descriptions of its dangers are exceedingly valuable, and have not always been enriched, but rather obscured by much of the work of subsequent observers. An exact pharmacological knowledge has only been obtained, however, by the studies of the past few years, and one of the reasons for this has been the lack of an exact physiological knowledge of the action of the heart.

The cardiac muscular mass maintains, when furnished with proper supplies of salts, oxygen, and foodstuffs, an automatic activity. Each cell, and hence the whole mass, may be considered as possessing the following physiological properties: irritability, contractivity, ryhthmicity, conductivity, and tone. The functioning of the whole heart may be influenced either by the cardiac centre, through the vagus and sympathetic nerves, or by chemical changes occurring in the heart muscle. The vagus nerve carries fibers, which, when stimulated, may depress each and all of the physiological properties referred to above; the most evident fact is the decrease in rhythm and contractivity. Drug stuffs may introduce such chemical changes in the muscle cell that any one of these properties is affected alone, or several of them at the same time, but not necessarily to the same